COMPARATIVE STUDY OF OCULAR MANIFESTATIONS OF MULTIPLE SCLEROSIS IN TWO AGE GROUPS; 16 - 30 AND 31 -51 YEARS IN YAZD, IRAN FROM 2002 TILL 2005

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SUMMARY: Multiple sclerosis (MS) is one of those groups of diseases whose peculiarity is demyelination of the white matter of the central nervous system. Ocular disorders are one of the most common manifestations of the disease. The present study was therefore done to evaluate ocular complications in multiple sclerosis.

This was a cross sectional observational study that included 50 multiple sclerosis patients referring to the ophthalmology and neurology clinics and departments affiliated to the Yazd, Medical Sciences University. All data was entered in a computer via SPSS software and analyzed by Chi-square and ANOVA statistical tests, thus results less than 0.05 was significant.

Of the total, 16 (32%) were men and 34(68%) were women. The most frequent complication in the population under study was optic neuritis that was present in 30 patients (60%), nystagmus was present in 14 cases (28 %) and diplopia in 9 cases (18%).

In the present study, optic neuritis was seen in 60 % (almost all cases with ocular pain and dischromatopsia), nystagmus in 28% and diplopia in 18% of the patients.

Key Words: Multiple Sclerosis, Optic Neuritis, Diplopia, Nystagmus, Loss of Vision.

INTRODUCTION

Multiple sclerosis is one of those groups of diseases whose peculiarity is demyelination of the white matter of the central nervous system (1). In this disease, myelin is inflamed and destroyed in the form of either singular or numerous, small or big plaques (2). The most common age of manifestation of this disease is between 20 and 35 years with its peak at 30 years (1, 2). Therefore, the population under study was divided into two age groups of 16-30 and 31-51 years even though cases have been reported in children and senile patients. Ocular disorders are one of the most common manifestations of the disease, such that about 25% of these patients have some sort of ophthalmologic involvement during the course of the disease (1, 2). These disorders include nystagmus and/or double vision which is sometimes accompanied with vertigo, intranuclear opthalmoplegia which if bilateral almost confirms the diagnosis, unilateral or bilateral loss of vision due to optic neuritis or papillitis (one third of cases have papillitis with varying degrees of disc

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Table 1: Distribution of ocular and neural findings according to gender.

Type of Complication		Men	Women	Total	p value
Optic Neuritis	Number	7	23	30	0.1
	Percent	43.8	67.6	43.8	
Retro and/or peri bulbar pain	Number	8	12	20	0.6
	Percent	50	35.3	40	
Dischromatopsia	Number	7	8	15	0.4
	Percent	43.7	34.7	30	
Interanuclear Ophthalmoplegia	Number	-	1	1	0.9
	Percent	-	2.94	2	
Diplopia	Number	3	6	9	0.6
	Percent	18.8	17.6	18	
Nystagmus	Number	6	8	14	0.3
	Percent	37.5	23.5	28	
Movement Disorder	Number	12	22	34	0.4
	Percent	75	64.7	68	
Sensory Disorder	Number	8	15	23	0.6
	Percent	50	44.1	46	
Balance Disorder	Number	6	10	16	0.5
	Percent	37.5	29.4	32	
Sphincter Disorder	Number	2	7	9	0.6
	Percent	12.5	20.6	18	
Total	Number	16	34	50	-

edema), majority of which are accompanied with peri or retro bulbar pain during eye movement, sometimes ptosis, uveitis and tangling of the retinal veins and rarely loss of vision due to chiasmal or retro chiasmal disorders and paralysis of the IIIrd, IVth and VIth cranial nerves. One of the common and important ocular manifestations of the disease is unilateral optic neuritis which can progress within a few hours or days and is seen in 50 - 70% of the cases. It is usually seen during the primary stages of the disease and lasts for one to three weeks (usually two weeks), but regression can take 4 - 6 weeks. Patients in whom optic neuritis is the primary manifestation have a comparatively better prognosis than others (2). Complications of optic neuritis include mild bleeding of the optic disc, impaired color vision, impaired field of vision and poor response of the pupils to normal light and narrowing in intense light. Even though this stage of the disease usually does not last for more than 2 weeks, some of the ophthalmologic problems like impaired color vision can last for a lifetime (2). There have many studies to date regarding the ophthalmologic complications of multiple sclerosis, but the number of studies in this field is very limited in Iran. Considering the importance of the topic and the fact that in most of the cases, the primary manifestations are ophthalmologic or it can be claimed that in special conditions, there are chances of not considering the ophthalmic manifestations as signs and symptoms of multiple sclerosis or probably misdiagnosing in few cases and not considering the disease, authors decided to study all the aspects of the ocular manifestations of multiple sclerosis referred to the related clinics and departments.

Table 2: Distribution of ocular and neural disorders findings according to age groups.

Type of Complication		Men	Women	Total	p value
Optic Neuritis	Number	16	14	20	0.9
	Percent	59.3	60.9	40	
Retro and/or peri bulbar pain	Number	8	12	20	0.6
	Percent	29.6	52.1	40	
Dischromatopsia	Number	6	9	15	0,4
	Percent	40	60	30	
Interanuclear Ophthalmoplegia	Number	-	1	1	0.9
	Percent	-	4.34	2	
Diplopia	Number	4	5	9	0.7
	Percent	14.8	21,7	18	
Nystagmus	Number	5	9	14	0.1
	Percent	18.5	39.1	28.8	
Movement Disorder	Number	16	18	38	0.1
	Percent	59.3	78.3	64	
Sensory Disorder	Number	15	8	23	0.1
	Percent	55.6	34.8	46	
Balance Disorder	Number	10	6	16	0.4
	Percent	37	26.1	32	
Total	Number	27	23	50	-
	Percent	100	100	100	

MATERIALS AND METHODS

This was a cross sectional observational study that included 50 multiple sclerosis patients. All data were abstracted from patients records totally. As there is no official estimate of the prevalence of the disease in the state of Yazd or Iran and other similar studies elsewhere have studied often between 3 - 50 patients, 50 patients referred or introduced to the ophthalmologic and neurological clinics of Yazd Medical University were included in the study. Ophthalmologic signs studied included; history of previous diseases, mode of involvement of the eyes including optic neuritis, papillitis, diplopia, nystagmus, intranuclear ophthalmoplegia, etc. Clinical examination included; slit lamp examination, opthalmoscopy, refraction, motility, pupil light reflexes, time of start and degree of loss of vision, sudden or gradual loss of vision, impaired color vision and pain during ocular movements. Neurological signs included; decreased sense of perception, decreased activity of sensory, motor and cerebellar systems, decreased urinary, intestinal and sexual systems activities. Para clinical neurological and ophthalmologic examinations included; MRI scans of the nervous system and spinal cord in all of the patients which was positive in 95% of the patients and plaques were present in around the lateral ventricles (90%) and corpus callosum, CT scan in certain cases wherein plaques were seen in 20% of the cases, VEP which was positive in 85% cases of optic neuritis, as well as EEG in patients with history of convulsions, perimetry to show a central scotoma (Kinetic) and/or scattered defects in the peripheral fields (Static), cerebrospinal fluid (CSF) examination to check increased immunoglobulin levels (IgG levels more than 20% of the total volume). All of the examinations were done with taking into consideration of all the ethical issues till to reach the diagnostic according to MC Donald,s criteria in which focuses on clinical, laboratory and radiologic data, nearly 85% of individuals were in relapsing remitting subtype also the other subgroups such as secondary progressive, primary progressive and progressive relapsing described and in cases where diagnosis could not be confirmed or there was a probability of peripheral nerve involvement (peripheral neuropathy), the cases were

excluded from the study as peripheral nerves are not involved in multiple sclerosis (MS) all of the diagnosed cases has been treated with specific category (3days intravenous corticosteroid then followed 11days orally). Even though ethnic, genetic factors and attitude can play an important role in this disease, they were not studied completely and there seems to be no significant difference between Yazd and other states of Iran. A special questionnaire and clinical examination was used to study multiple sclerosis patients from March, 2002 till end of February, 2005 to reach the desired number of patients. Variables like age, sex, number of attacks of MS (one to six times), time period of affliction (0-1 year, 2-3 years, 4-17 years), unilateral or bilateral ocular involvement (Right eye, left eye or both eyes) were entered in SPSS software program and chi square and Variance analysis statistical tests were used for evaluation. All probability less than 0.05 was considered significant. Consideration of work restrictions like low number of patients, incomplete history and compliance of patients was essential.

RESULTS

In the present study, 50 multiple sclerosis patients comprising of 16 men (32%) and 34 women (68%) were serially included in the study. Of the total, 21 cases (42%) had right eye involvement, 20 cases (40%) had left eye involvement and 9 cases (18%) had no ocular involvement. The most frequent complication in the population under study was optic neuritis that was present in 30 patients (60%) of which 24 cases (80%) were unilateral and 6 cases (20%) were bilateral. It presented as retro bulbar optic neuritis in 23 patients (76.6%) and papillitis in 7 cases (23.4%) , of which 20 cases (66%) in whom decrease in vision in the initial 2-3 days was not less than 20/200 had sudden loss of vision and 10 cases (33%) had gradual loss of vision. In addition, disordered pupil light reflex between 1+ and 3+ was seen in 70% cases which lasted for approximately 2 weeks. Nystagmus was seen in 14 cases (28%) of which 11 cases (22%) were horizontal, 2 cases (4%) were rotational and 1 case (2%) was rotational and vertical. Diplopia was seen in 9 cases (18%) with lateral rectus paralysis in 5 cases (10%) and medial rectus paralysis in 4 cases (8%). Of the total, 1 case (2%) have had interanuclear ophthalmoplegia. 20 patients (40%) of which 8 cases (40%) were men and 12 cases (60%) were women had peri and retro bulbar pain. Dischromatopsia and decreased contrast sensitivity was seen in 15 cases (30%) of which 8 patients (53.3%) were women and 7 patients (46.7%) were men.

Of the total, 34 patients (68%) had impaired movement, 23 patients (46%) had sensory impairment, 16 patients (32%) had dynamic equilibrium disorders and 9 patients (18%) had sphincter disorders, so the distribution of ocular and sensory disorders according to gender as well as statistical analysis (P Value) presented in (Table 1).

Regarding distribution of ocular and sensory complications according to age, the youngest patient was 16 years old, oldest patient was 51 years old and 5 patients (10%) were around 24 years of age. The population under study was divided into two age groups; 16 -30 years comprising of 27 patients (54%) and 31 - 51 years comprising of 23 patients (46%). Of the 30 patients with optic neuritis, 16 cases (60.9%) were in the 16 - 30 years age group and 14 cases (59.1%) were in the 31 - 51 years age group. Regarding distribution of ocular disorders, most of the patients were in the 31 - 51 years age group. as well as motor weakness and sphincter disorders were more in the 31 - 51 years age group, but sensory, neural and balance disorders were more in the 16 - 30 years age group, distribution of ocular and sensory disorders according to the age groups also statistical evaluation (P Value) presented in (Table No.2). Time period since start of disease ranged between 1 - 17 years and patients were divided into three groups; 28% in Group I (0 -1 year), 34% in Group II (2 - 3 years) and 38% in Group III (4 - 17 years).

Of the 30 patients with optic neuritis, 24 cases (80%) had unilateral eye involvement with almost equal involvement of both the right and left eye and 6 cases (20%) had bilateral eye involvement. Diplopia was present in 9 cases (18%) and nystagmus in 14 cases (28%). The number of attacks ranged between 1 - 6 and the greatest (28%) had 1-2 attacks, while only 2% had 6 attacks. Most complications were seen in women affected chronically, rate of complications was directly related to time period of affliction and most of the complications were seen in the 31 - 51 years age group.

DISCUSSION

The present study was done in order to evaluate the ocular features of multiple sclerosis (MS). As understood from various studies, MS usually presents with ocular manifestations. In the present study, of the 50 patient's studied, 82% had ocular involvement since the start of the disease or during its course and 18% had no ophthalmic involvement.

Adams and co workers in 1997 showed that just as MS is a disease of the young, ocular complications of the disease are also more in the young. They determined the age range to be between 20 -40 years, in our study the age range was between 16 - 51 years, so that is somewhat similar to their study (1). Mathews (3) in 1996 described MS disease and its ocular manifestations such as vision and motility disorders and used prednisolone to treatment the patients , in the present study ocular sign had priority and corticosteroide used for treatment of all the cases which is in line with above study in some directions .

Steinlin and co workers (4) in 1995 in a retrospective study on 17 children afflicted with MS in Toronto, Canada observed that 94% (16 of the total of 17 children) had ophthalmic manifestations of which 47% had minor disorders, 12 children had optic neuritis and 4 had 6th nerve palsy with interanuclear ophthalmoplegia, in addition the study reported ophthalmic manifestations to be more chronic in children as compared to adults, while the minimum age of patients in the present study was 16 years and the studies were similar only in respect to optic neuritis.

Morales and co-workers (5) in 2000 studied 150 patients with a mean age of 12 years suffering from MS and realized that 60% were girls and 40% were boys. In the present study, 68% were women, 32% were men and all the complications were more in women. The study concluded that in this age group, prognosis is better in those with unilateral ophthalmic involvement and most of them attain 20/40 visual acuity. Those with bilateral optic neuritis (66%) usually present as papillitis which is not similar to the present study.

Jin and co-workers (6) in 1998 reported ophthalmic complications have a peak in two groups of 30-34 years and 45-49 years. In the present study, there were groups; 16-30 years and 31-51 years but the greatest affected number was around 24 years.

Soderstrom (7) in 2001 reported that optic neuritis usually presents acutely and unilaterally and this affects the type of treatment. In addition, regarding the effect of time period of affliction on complications of MS, results show that with an increase in the chronicity of the disease, the complications also increase of which optic neuritis (63.2%) and movement disorders (84.2%) are the maximum. In the present study, optic neuritis which was usually acute and unilateral was present in 60% of the cases and movement disorders were present in 68% of the cases. Regarding time period of affliction too, the studies are in line with each other as cases with affliction of 4-17 years had the maximum number of complications.

Deya and co-workers (8) in 1999 studied the ophthalmic complications of 28 MS patients and found out that all of them were in the 18-45 years age group and had unilateral optic neuritis. After treatment, 24 recovered completely. In the present study, the age range was 16-51 years and 80% had unilateral optic neuritis and medication was mostly effective which is somewhat similar to the above study.

Phadke (9) in 1987 stated that as the disease becomes more chronic, especially more than 25 years, the debilitating complications also increase. In the present study, maximum complications were present in patients suffering between 4-17 years.

In the study by Granadier (10) in 2000 on MS patients, it was determined that optic neuritis is the most common ophthalmic complication and a leading cause of loss of vision. It presents as sudden loss of vision and painful movements of the eyeball which becomes better within a few months. In the present study, 60% had optic neuritis of which 66% had sudden loss of vision, painful eye movements and a type of color vision disorder.

Frederickson and co-workers (11) in 1996 studied 233 women suffering from acute optic neuritis realized that 161 patients (69%) were suffering from retro bulbar optic neuritis and 62 patients (26.6%) were suffering from papillitis. The mean age in these two groups was 33 years. In the subsequent follow up, there was no major difference between retro bulbar optic neuritis and papillitis. This was due to the fact that both retro bulbar optic neuritis and papillitis were both a part of the spectrum of MS and both can be treated by one line of treatment. In the present study, optic neuritis presented as retro bulbar palsy in 23 cases (76.6%) and papillitis in 7 cases (23.4%) which is nearly like the above study.

Barton (12) in 1993 studied 37 pendular nystagmus patients and reported that all of the patients had cerebellar presentations and ophthalmic involvement such that 18 cases of the 37 patients (48.6%) had asymmetrical nystagmus due to asymmetrical optic neuropathy. In the present study, 28% of he patients had nystagmus of which 11 cases (22 had pendular nystagmus, 4% rotational and 2% had concurrent vertical and rotational nystagmus. Pendular nystagmus was the most common type of nystagmus in the study.

Uitti (13) in 1986 stated that diplopia in MS patients is due to involvement of the 6th cranial nerve. Even though interanuclear ophthalmoplegia can result in diplopia, involvement of the third and fourth cranial nerve is rare. In that study, the right external rectus muscle (VIth nerve) was mostly involved in diplopia and in the present study too, of the 18% of the cases who had diplopia, 10% had right external rectus muscle involvement (5 cases) and 8% (4 cases) had left external rectus muscle involvement.

The relation between the number of attacks and complications was studied in the present study, of the total, 28% had 1-2 attacks, 26% had 3 attacks, 4% had 4 attacks, 12% 5 attacks and 2% had 6 attacks, the maximum number of complications was seen in those with history of 3 attacks except dynamic equilibrium disorders which were more in those with history of 2 episodes, all of the other complications wee more in those with history of 3 episodes, with each episode, an extra complication which could be either ophthalmologic or non ophthalmologic had occurred, but there was no significant relationship between the number of attacks and severity of complications and there were no other similar studies for reference in this field.

CONCLUSION

In the present study, 50 Multiple Sclerosis (MS) patients in the age range of 16 - 51 years (16-30 years and 31-51 years) were studied. Of the total, 30 cases had optic neuritis of which 24 (80%) was unilateral and 6 (20%) was bilateral. 23 cases (76.6%) presented as retro bulbar optic neuritis and 7 cases (23.4%) as papillitis, also 15 cases (30%) had dischromatopsia, 20 cases (40%) had retro bulbar pain especially during eye movement, diplopia in 9 cases (18%) with maximum involvement of lateral rectus muscle, nystagmus in 14 cases (28%) pendular being the most common form, there were no ophthalmologic complications in 9 cases (18%), movement disorders were seen in 68%, sensory disorders in 32% and balance disorders in 18% of the cases, women were more affected than men with a peak of onset at 24 years of age, number of bouts or attacks were 1-6 and most of the patients had had 3 attacks.

REFERENCES

1. Adams Raymond D, Victor Maurice, Allan H Ropper, Roberth Brown: Principle of neurology. 8th edition- part 4; chapter 36, 771-781, 2005.

2. Alastair Compston, George Ebers, Hans lassmann, Ian McDonald, Bryan Matthews, Hartmutt Wekerle, Mc Alpine's: Multiple Sclerosis. 3rd edition, Churchill Livingstone, 157-158, 1999.

3. Mathews DE: What is your diagnosis? Multiple Sclerosis. Optom Clin, 5(3-4): 193-203, 1996.

4. Steinlin MI, Blaster SI, Mac Gregor DI, Buncic JR: Eye problem in children with multiple sclerosis. Pediatr Neurol, 12(3): 207-212, 1995.

5. Morales DS, Siatkowski RM, Howard CW, Warman R: Optic neuritis in children. J Pediatr Ophthalmol strabismus, 37(5) 254-259, 2000.

6. Jin Y de pedro, Cuestu J, Soderstorm M, Stawiarz L, Link H : Seasonal pattern in optic neuritis and multiple sclerosis. J Neurol Sci, Dec 1,181(1-2) : 56-64, 2000.

7. Soderstrom M: Optic neuritis and multiple sclerosis. Acta Ophthalmol Scand, 79(3):223-227, 2001.

8. Deya E, Sevilla T, Coret F: A risk of developing multiple sclerosis following an outbreak of optic neuritis during a mean follow up of 4.5 years. Neurologia, 13(8): 377-381, 1998.

9. Phadke JG, Downie AW: Epidemiology of multiple sclerosis in the north east (Grampion Region) of Scotland and update; Journal of epidemiology and community health, 41:5-13, 1987.

10. Granadier Rj: Ophthalmology update for primary practitioners. part I, Update on optic neuritis Dis Mon, 46(8):508-532, 2000.

11. Frederickson JL, Olsen J, Larsson HB, Petera J, Sellebjerg FT: Acute unilateral Papillitis versus retro bulbar neuritis: relation to multiple sclerosis. Mult Scler, 1(4): 223-227, 1996.

12. Barton JJ, Cox TA: Acquired convergence evoked pendular nystagmus in multiple sclerosis: Clinical observations and the rule of optic neuropathy. J Neural, Neurosurg, Psychiatry, 56(3):262-267, 1993.

13. Uitti RJ, Rajput AH: Multiple sclerosis presenting as isolated oculomotor palsy. Canadian Journal of Neurological Science 13:270-272, 1986.

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